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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/405,120	03/16/95	BATCHELOR	K

EXAMINER
DAVIS, D

12M2/1124

ART UNIT	PAPER NUMBER
1202	5

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DATE MAILED: 11/24/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☑ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☑ Claims 1-24 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☑ Claims 1-24 are rejected.

5. ☐ Claims _____ are objected to.

6. ☑ Claims 1-24 are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

Is applicant waiving benefit of SN 123,280? If not, amendment inserting mention is required by 35 USC 120.

Applicants' information disclosure statement has been received.

A copy of the PCT gazette page is required for the printer, a copy of the WO document is requested-Depending on its print date it may be competent as a reference.

Copies of references in the specification and not previously supplied are requested if pertinent to the claims.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1 to 24 are in the case rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The following reasons apply:

1. Is there an extra 0 in claims 22-3? Is Cox intended? (par 2).

2. What is an "~~answer~~ androgen responsive or mediated disease"? (par 2) Term isn't defined in Specification. (par 1) Is prostate cancer intended?

3. (Claim 9) "Baldness" and "hirsutism" are not diseases, so claim 9 is improperly dependent - ie not embraced by claim 8, obscuring intent of each, (par 2).

4. (Claims all) No reasonable assurance is seen that the compound embraced is useful for benign hyperplastic of prostate. Stinson reports that the one compound cleared for such use is less than 50% effective for alleviating symptoms. (No data are provided herein) Marzocchi. (par. 1)

5. (Claims , 9) No teaching "how to use" for benign hyperplastic of prostate is described herein. In view of Stinson report, even if dose is known (unlike instantly) undue experimentation is required, in re Wands 8 USPQ 21 1400 Specification must teach "how to use", not how to find out "how to use. In re Gardner 166USPQ 138 (par. 1)

6. (Claims 8, 9) No reasonable assurance is seen the compound is useful for alopecia. Helicker article evidences there is no universal treatment for almost all patients. The Diani article provided is further evidence.

Diani, p. 345, in 1992 states "5a reductase inhibitors have not been evaluated in androgenetic alopecia patients... It is not known whether inhibition of the 5a reductase system can grow hair in the balding stumptail monkey or humans". Marzocchi. (par.1)

7. (Claims 8-21) What is intended by "safe and effective" ~~11~~? (por 2)

Term is non-limiting and indefinite as to nature of disorder and criteria for "effective". Stinson reports less than 50% effectiveness. Is this intended? Similarly no criteria for safety are seen.

8. (Claims 8, 9) The specification does not describe "how to use" for baldness. No test data in support thereof are seen. See In re Oberweger 47 USPQ 455, In re Ferens, 163 USPQ 609.

Even certain salts of Monoxidil have been found inoperative. Upjohn v. Riahorn Corp. 1 USPQ 2d 433, Upjohn v. Medron 17 USPQ 2d 1268. The Diani and Helicker articles show the art does not know "how to use" compounds for alopecia. Specification must teach "how to use" not how to find out "how to use". In re Gardner 166 USPQ 138. Disclosure does not provide specific benefit in currently available form. Brenner v. Manson 148 USPQ 689, Cf. In re Colianni 195 USPQ 150 (par. 1).

9. No criteria are described for "effective" amount" in claim 7. How does the rabbit or rat indicate to its vet (or human to his/her medic) that the amount administered is "effective" i.e. that some, both or one of its 5 alpha reductase is inhibited.

(Particularly to female patients). As in vitro property isn't necessarily a utility in vivo in currently available form Brenner v. Manson (par. 1) Are unsafe" effective amounts intended? (par 2).

10. No description "how to use" for hirsuteness is seen in the specification, The same dosage for baldness? (par. 1) Gardner. What is compounds' effect on female "Mexican hairless dogs"? (par. 1)

11. No therapeutic indications for claim 7 are provided in the specification. I.e. What criteria are used by the medic/vet to determine patient need as well as effectiveness. No enabling guidance is seen in the specification. (par. 1)

12. No teaching "how to make" or use claims 22-3 compounds is described. (par. 1)

13. (Claims 8, 9) No teaching "how to use" compounds to treat prostate cancer is described in the specification. Is it used with radiation? With 5FU? (par. 1)

14. In view of the dearth of compounds known to treat prostate cancer and the highly empirical nature of cancer treatment, no reasonable assurance is seen instant compound actually treats prostrated cancer. Marzocchi. Cf. In re Jolles 206 USPQ 885 where closely related cancer treating compounds had FDA clearance. In re Hozumi 226 USPQ 353. (par. 1)

15. (Claims 12, 15, 19) what "alpha 1 adrenegic blockers" are intended? What "antiestrogens "are intended? What "antiandrogen? (Arent alpha reductase ~~intended~~ inhibitors antiandrogens? (par 2) No

definitations are seen (par 1) to 21.

16. (Claims 1-3, 7 to 21) What solvents are intended in "solvates"? Acetone? Water? Isopropanol? DMSO? DMF? (par 2) specification provides no guidance (par 1)

2) What is "aryl comprises"?

17. (Claims 7-9) No teaching "how to use" compound for both hirsutism and baldness since the results are opposite, does it gorw hair on the head but inhibit the chest hairs? What effect does it have on "mexican hairless" dogs male or female? Specification provides no guidance.

Undue experimentation is needed to determine What dosage level causes which result on which gender subject employed. Does it restore hair to chemotherapy patents? (par 1) 18 (claims 16-17) are unsafe/toxic amounts of Tamoxifen intended? (par 2) 19. No teaching enabling how to use ARi conbined with toxic anti estrogen is described. (par 1)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claim 25 is rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Biozhaz.

See Ex. 11.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 22-3 are rejected under 35 U.S.C. § 102(e) as being anticipated by Biollaz.

Claim 3 is rejected as the obvious method for making a mixture. In re Becket 33 USPQ 33.

Claims 4-6 are rejected under 35 U.S.C. § 103 as being unpatentable over Kojima EP '094.

Ex 1, 2, 7, 19, 87, e.g. teach anolopus reactions "B" using various conditions. See also Reaction A. Reaction B suggests use of acyl halides.

Reaction C therein discloses 4 methods of accomplishing analogous reaction A.

The use of analogs in known conventional processes is not ordinarily patentable. In re Durden 226 USPQ357,

The very terms of instant claims admit/suggest conventionality.

Claims 4-6 are rejected under 35 U.S.C. § 103 as being unpatentable over Rasonusson 071.

Examples 1 teaches Reaction A dehydrogenation Ex. 2/25D, 5E teach analogous amide formation, Reaction D. Use of substituted arylamines is suggested, col 2, lines 41-46. Durden

Claims 1-3, 7-11 are rejected under 35 U.S.C. § 103 as being unpatentable over Rasmusson' 071.

Col 1, lines 25-28 teach dihalo and xylyl, (dimethyl) anilides as ARIs. One would expect di (halomethyl) anilides and di (trihalo methyl) anilides are also ARIs. See abstract, col 5 lines 63-69. Applicants admit, page 6, the particular ~~amyluria~~ aniline is commercially available. Its choice is mutren the skill of the art.

Claims 22-4 are rejected under 35 U.S.C. § 103 as being unpatentable over Rasmusson 071.

See col 6, structures X, XI since acyl halides also react with aryl amines to form arylamides, and ~~since~~ X is often used to represent halogens, structure X suggests claim 24 compound, useful for the reference purpose.

Claims 1-3, 7-11, 18-21 are rejected under 35 U.S.C. § 103 as being unpatentable over Gormley WO 233.

Page 17 teach anibides where the phenyl can be substituted by methyl or halo. Halomethyl analogs would be expected to retain ARI activity, claims 1, 2 claims teach ARI combined with Flutamide

for a particular prostate malady.

Claims 1-3, 7-15, are rejected under 35 U.S.C. § 103 as being unpatentable over Gormley WO 213.

Page 7 discloses anilides with methyl as halo substitutents that are ARIs. Halomethyl analog would be expected to retain activity, Ex5, 6, pages 192-3 teaches preparation of anilide analogs. See claims 1, 2 for concept of coadministration with alph 1 adrenergic blocker.

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1 to 4, 6, 10 are, drawn to compounds and simple compositions, classified in Class 546, subclass 577 and 514/284.

II. Claims 5-7, drawn to multiple processes for I, classified in Class 546, subclass 77.

III Claims 8, 9, 11, multiple methods of Using I

~~Newly submitted claims 7-9, 11 are directed to an invention~~ that is independent or distinct from the invention originally claimed for the following reasons: multiple methods of using I

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 514 withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. ~~§ 1.142(b) and M.P.E.P. § 821.03.~~

IV. Claims 12-14, 16-7, 19-20, drawn to compositions with I plus (a) alpha 1 adrenergics or (b) anti estrogen (c) anti

androgens, classified in Class 514, subclass 284.

V. Claims 15, 18, 21, drawn to multiple methods of using III (a) (b) or (c), classified in Class 514, subclass 284.

VI. Claims 22-4, drawn to intermediates, classified in Class 546, subclass 77.

Biollaz evidences no "special technical feature" is present for all inventions.

If III or V is elected, a single use of a single compositions, I, III a, IIIb or IV(c) must be further elected.

(To aid applicants choice, if I is elected, its use for acne may be examined, therewith a claim limited thereto is presented).

If II is elected, a single non alternative process must be further elected.

I can be made other than via VI, ie the using analogous pyridyl thio ester. IV can be (and is) used, to make Biollaz compounds. Iand VI are independent, of applicants would not acquence in art anticipating VI rendering I obvious. They are independent.

I does not depend on any single process of II, being independent thereof.

The processes are patentably distinct. If I or VI were allowable, it doesn't follow that any and of II processes would be Durden MPEP 806.05(f) anthorizes restriction, Formley WO's show the same compounds combined with different W active ingredients do support separate patents, form the single ingredient azasteroind

(CF Merck EP's, WO's) Different issues of patentability (eg ennoblement) arise.

Different issues of ennoblement arise for the multiplicity of uses claimed. Even were the composition anticipated, a novel use (IF enabled) may still be patentable, In re May 198 USPQ 601 MPEP 806.05(h) authorizes this restriction.

The inventions as grouped are independent, distinct and lack a common special technical feature not shared with the art (e.g Bollaz).

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

Daus:nps
November 20, 1995

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